

Award Number: W81XWH-10-1-0627

TITLE : "Laser Applications on Orthopaedic Bone Repair"

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REPORT DATE: March 2012

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
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1. REPORT DATE (DD-MM-YYYY) March 2012		2. REPORT TYPE Annual		3. DATES COVERED (From - To) 1 Sep 2011 - 29 FEB 2012	
4. TITLE AND SUBTITLE "Laser Applications on Orthopaedic Bone Repair"				5a. CONTRACT NUMBER W81XWH-10-1-0627	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Kotaro Sena, D.D.S., Ph.D.; Amarjit S. Viridi, Ph.D. email: Jennifer_Garcia@rush.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Rush University Medical Center 1653 W Congress Pkwy. Chicago, IL 60612-3839				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The goal of this project is to improve the treatment of bone defect by leveraging a rat cortical bone allograft model and Er:YAG laser currently used in the dental field. To achieve this goal we will test the hypothesis that: 1) segmental bone defects treated with Er:YAG laser irradiation will form significantly more and stronger cortical bone allograft incorporation; and 2) segmental bone defects treated with cortical bone allograft pre-conditioned by Er:YAG laser will form significantly more and stronger cortical bone allograft incorporation. The project is currently in progress and definitive results await further analysis. However, post-operative observations and body weight gain indicated there were no complications such as allergic reactions, abscesses or infections. Body weight gain in the laser-treated animals was similar to that in non-laser treated animals during the healing period. These results showed a successful feasibility of the Er:YAG laser system for the cortical bone allograft model.					
15. SUBJECT TERMS erbium:YAG (Er:YAG) laser, bone allograft, bone repair					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 11	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

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INTRODUCTION

It has been reported that more than 30,000 American service members have been wounded in the wars in Iraq and Afghanistan during the last six years. The majority of service members who are wounded in action sustain musculoskeletal injuries such as the orthopedic-related trauma involving the upper and lower extremities present with a significant bone defect. Bone allografts have become an accepted technology to replace bone loss. However, major complications reported for grafting procedures are infection, bone graft fracture, non-union at the graft-host interface, and, rarely, massive allograft resorption. Recent advances in technology have led to a development of novel approaches for use of lasers in hard tissue surgeries in the dental field. The laser that show the most promise for hard tissue surgery is the erbium:YAG (Er:YAG) laser. Recent reports indicates Er:YAG laser provides; (1) advantageous bone surface for bone tissue repair; (2) bactericidal effect; (3) applications for both soft and hard tissue. However, it has not been shown whether Er:YAG laser has a positive effect on orthopedic bone repair. The goal of this project is to improve the treatment of bone defect by leveraging a rat cortical bone allograft model and Er:YAG laser currently used in the dental field. We hypothesis that: 1) allograft bed treated with Er:YAG laser irradiation will lead to more and stronger cortical bone allograft incorporation; and 2) segmental bone defects treated with cortical bone allograft pre-conditioned by Er:YAG laser will lead to more and stronger cortical bone allograft incorporation. The project is currently in progress and definitive results await further analysis. However, post-operative observations and body weight gain indicated there were no complications such as allergic reactions, abscesses or infections. Body weight gain in the laser-treated animals was similar to that in non-laser treated animals during the healing period. These results showed a successful feasibility of the Er:YAG laser system for the cortical bone allograft model. Samples are currently under investigation for micro CT analysis and mechanical testing.

BODY

The following is a summary of the work completed to the present time based on the project's accepted Statement of Work. Comments by PI follow below.

Statement of Work

Task 1: Determine the effect of Er:YAG laser on allograft bed.

1a. Preparation for the animal study - completed

Obtain animal use approvals and order the supplies.

1b. Preparation of the allografts - completed

Obtain cortical bone grafts from the donor rats (n=26; 2 grafts/animal) prior to the surgery. Allografts will be sterilized with 70% ethanol and then fresh frozen at -80°C until use.

1c. Perform surgery – harvest after 4 & 8 week post-surgery - completed

Perform surgery; create segmental defect (n=78) and utilize cortical bone allograft grafts (n=52) prepared above (1b). Some animals (group 2 & 7) will undergo laser irradiation during the surgery. Four and 8 weeks post-surgery, for mechanical testing, the dissected bones will be wrapped in saline soaked gauze and frozen at -20°C. For undecalcified histology, the dissected bones will be fixed in 10% neutral buffered formalin.

1d. Analyze the samples - in progress

Analyze the samples by μ CT, mechanical test and histology.

Task 2: Determine the effect of Er:YAG laser on allograft.

2a. Preparation for the animal study - completed

Obtain animal use approvals and order the supplies.

2b. Preparation of the allografts - completed

Obtain cortical bone grafts from the donor rats (n=26; 2 grafts/animal) prior to the surgery. Allografts will be sterilized with 70% ethanol and then fresh frozen at -80°C until use. Some allografts (for group 3, 4, 8, and 9) will undergo laser irradiation prior to the surgery.

2c. Perform surgery - harvest after 4 & 8 week post-surgery - **completed**

Perform surgery; create segmental defect (n=52) and utilize cortical bone allograft grafts (n=52) prepared above (2b). Some animals (group 4 & 9) will undergo laser irradiation during the surgery. Four and 8 weeks post-surgery, for mechanical testing, the dissected bones will be wrapped in saline soaked gauze and frozen at -20°C. For undecalcified histology, the dissected bones will be fixed in 10% neutral buffered formalin.

2d. Analyze the samples - **in progress**

Analyze the samples by μ CT, mechanical test and histology.

Comments:

The project is currently in progress and definitive results await further analysis. However, post-operative observations and body weight gain indicated there were no complications such as allergic reactions, abscesses or infections. Body weight gain in the laser-treated animals was similar to that in non-laser treated animals during the healing period. These results showed a successful feasibility of the Er:YAG laser system for the cortical bone allograft model. Contact X ray images obtained during the healing period indicate similar or larger callus in laser-treated groups compared to non-treated groups. However, these qualitative observations are done in two-dimensional, projected image while subsequent micro CT analysis will provide better understanding in three-dimensions. Moreover, mechanical testing is the primary endpoint for the project which will be performed after non-destructive-X ray analysis. Project is extended for additional 6 months to complete the sample analysis and manuscript preparation.

KEY RESEARCH ACCOMPLISHMENTS

- Completed all animal surgeries.
- No adverse effect or complication by use of Er:YAG laser in cortical allograft model.

REPORTABLE OUTCOMES

The investigators are currently awaiting results of ongoing analysis from the project. Following personnel received research training based on animal procedures in this research project which includes introduction and training for Er:YAG laser.

- Vbenosawemwinghaye Orhue, M.D. – Postdoctoral fellow
- David F. GomezGil, D.D.S., M.S. – Ph.D. candidate
- Siddhesh R. Angle, Ph.D. – Ph.D. candidate
- David G. Karwo, B.S. – Research assistant
- Julie E. Brown, B.S. – Research assistant

CONCLUSION

- There was no adverse effect or complication by use of Er:YAG laser in cortical allograft model.
- Project is extended for additional 6 months to complete the sample analysis and manuscript preparation.

APPENDICIES

1. Memorandum for the Record – Approval of extension (3/16/2012)

AMENDMENT OF SOLICITATION/MODIFICATION OF CONTRACT				1. CONTRACT ID CODE S		PAGE OF PAGES 1 2	
2. AMENDMENT/MODIFICATION NO. P00001		3. EFFECTIVE DATE 15-Mar-2012		4. REQUISITION/PURCHASE REQ. NO. W91ZSQ0122N678		5. PROJECT NO.(If applicable)	
6. ISSUED BY USA MED RESEARCH ACQ ACTIVITY 820 CHANDLER ST FORT DETRICK MD 21702-5014		CODE W81XWH		7. ADMINISTERED BY (If other than item 6) US ARMY MEDICAL RESEARCH ACQUISITION ACT ATTN: JOSHUA MCKEAN 301-619-4046 FORT DETRICK MD 21702		CODE W81XWH	
8. NAME AND ADDRESS OF CONTRACTOR (No., Street, County, State and Zip Code) RUSH UNIVERSITY MEDICAL CENTER RONALD NEFF 1653 W CONGRESS PKWY CHICAGO IL 60612-3839				9A. AMENDMENT OF SOLICITATION NO.			
				9B. DATED (SEE ITEM 11)			
				X 10A. MOD. OF CONTRACT/ORDER NO. W81XWH-10-1-0627			
				X 10B. DATED (SEE ITEM 13) 01-Sep-2010			
CODE 3F752		FACILITY CODE					
11. THIS ITEM ONLY APPLIES TO AMENDMENTS OF SOLICITATIONS							
<input type="checkbox"/> The above numbered solicitation is amended as set forth in Item 14. The hour and date specified for receipt of Offer <input type="checkbox"/> is extended, <input type="checkbox"/> is not extended. Offer must acknowledge receipt of this amendment prior to the hour and date specified in the solicitation or as amended by one of the following methods: (a) By completing Items 8 and 15, and returning _____ copies of the amendment; (b) By acknowledging receipt of this amendment on each copy of the offer submitted; or (c) By separate letter or telegram which includes a reference to the solicitation and amendment numbers. FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER. If by virtue of this amendment you desire to change an offer already submitted, such change may be made by telegram or letter, provided each telegram or letter makes reference to the solicitation and this amendment, and is received prior to the opening hour and date specified.							
12. ACCOUNTING AND APPROPRIATION DATA (If required)							
13. THIS ITEM APPLIES ONLY TO MODIFICATIONS OF CONTRACTS/ORDERS. IT MODIFIES THE CONTRACT/ORDER NO. AS DESCRIBED IN ITEM 14.							
A. THIS CHANGE ORDER IS ISSUED PURSUANT TO: (Specify authority) THE CHANGES SET FORTH IN ITEM 14 ARE MADE IN THE CONTRACT ORDER NO. IN ITEM 10A.							
B. THE ABOVE NUMBERED CONTRACT/ORDER IS MODIFIED TO REFLECT THE ADMINISTRATIVE CHANGES (such as changes in paying office, appropriation date, etc.) SET FORTH IN ITEM 14, PURSUANT TO THE AUTHORITY OF FAR 43.103(B).							
C. THIS SUPPLEMENTAL AGREEMENT IS ENTERED INTO PURSUANT TO AUTHORITY OF:							
X D. OTHER (Specify type of modification and authority) IAW USAMRAA General Terms and Conditions							
E. IMPORTANT: Contractor <input checked="" type="checkbox"/> is not, <input type="checkbox"/> is required to sign this document and return _____ copies to the issuing office.							
14. DESCRIPTION OF AMENDMENT/MODIFICATION (Organized by UCF section headings, including solicitation/contract subject matter where feasible.) Modification Control Number: jmckean123074 1. The purpose of this modification is to extend the period of performance, without additional funding, from 1 September 2010-31 March 2012 to 1 September 2010-30 September 2012 (research ending on 31 August 2012). 2. The final technical report originally scheduled for 31 March 2012 will now be submitted as an annual technical progress report. The final technical report will now be due on 30 September 2012. 3. All other terms and conditions of the award remain unchanged.							
Except as provided herein, all terms and conditions of the document referenced in Item 9A or 10A, as heretofore changed, remains unchanged and in full force and effect.							
15A. NAME AND TITLE OF SIGNER (Type or print)				16A. NAME AND TITLE OF CONTRACTING OFFICER (Type or print) SUSAN DELLINGER / CONTRACTING OFFICER TEL: 301-619-2090 EMAIL: susan.dellinger@amedd.army.mil			
15B. CONTRACTOR/OFFEROR (Signature of person authorized to sign)		15C. DATE SIGNED		16B. UNITED STATES OF AMERICA BY <u>Susan M. Dellinger</u> (Signature of Contracting Officer)		16C. DATE SIGNED 15-Mar-2012	

SECTION SF 30 BLOCK 14 CONTINUATION PAGE

SUMMARY OF CHANGES

SECTION 00010 - SOLICITATION CONTRACT FORM

CLIN 0001

The CLIN extended description has changed from Period of Performance: 1 September 2010-31 March 2012 (research ends 29 February 2012)Peer Reviewed Orthopaedic Research Program (PRORP)-Hypothesis Development Award to Period of Performance: 1 September 2010-30 September 2012 (research ends 31 August 2012)Peer Reviewed Orthopaedic Research Program (PRORP)-Hypothesis Development Award.

DELIVERIES AND PERFORMANCE

The following Delivery Schedule item for CLIN 0001 has been changed from:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
POP 01-SEP-2010 TO 31-MAR-2012	N/A	USA MED RESEARCH MAT CMD 1077 PATCHEL STREET BLDG 1056 FORT DETRICK MD 21702 FOB: Destination	W91ZSQ

To:

DELIVERY DATE	QUANTITY	SHIP TO ADDRESS	UIC
POP 01-SEP-2010 TO 30-SEP-2012	N/A	USA MED RESEARCH MAT CMD 1077 PATCHEL STREET BLDG 1077 FORT DETRICK MD 21702 FOB: Destination	W91ZSQ

(End of Summary of Changes)